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# Assessing Survival Times of Breast Cancer Patients Using Type I Generalized Half Logistic Survival Model

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Author POA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author AKO reviewed the study and the manuscript and author OAK helped in data collection and the ethical clearance. Author ORI wrote the conclusion and reviewed the results. All authors read and approved the final manuscript.*

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## ABSTRACT

In Nigeria, Breast Cancer is the most common malignancy among women. Unfortunately, many breast cancer patients present for treatment late. A Type I Generalized Half Logistic Survival Model was applied to a secondary data of eighty nine breast cancer patients collected from Ladoke Akintola University of Technology Teaching Hospital Osogbo. The study was focused on the 1-year survival of breast cancer patients from the day of presentation. Patient who were diagnosed with breast cancer from 2009 to 2014, were recorded. Age, stage of presentation, average years of

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breastfeeding, neoadjuvant treatment offered, age at menarche and use of contraceptives were the variables used in the study. The median survival time is 471 days. The contributions of the prognostic factors were assessed. The result showed that age at menarche and stage of presentation were significant at 0.05 level of significance while age of patients, average years of breastfeeding, use of contraceptives and neoadjuvant application were insignificant. Also, the accelerator factor between the early presented Breast Cancer patients and the late presented Breast Cancer patients was determined. The derived model was compared with the results of some common existing survival models, and this revealed that the type I generalized half-logistic survival model clearly demonstrates superiority over these other models.

*Keywords: Model; survival; half logistic distribution; breast cancer.*

## 1. INTRODUCTION

Cancer is known medically as a malignant neoplasm. It is a broad group of disease involving unregulated cell growth. In Cancer, cells divide and grow uncontrollably, forming malignant tumors and invading nearby parts of the body. The cancer may also spread to more distant parts of the body if not well taken care of at the early stage of formation. At an individual level, diagnosis of cancer is regarded as a human tragedy [1]. It is a leading cause of death worldwide, accounting for 7.6 million deaths (about 13% of deaths) in 2008 and is projected to continue rising with an estimate of 13.1 millions death in 2030 [2].

There are over two hundred different known cancers that affect humans but findings show that the commonest is Breast Cancer [3].

Breast cancer is when cancer develops from breast tissue. Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, or a red scaly patch of skin. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or spinal cord paralysis. With 1 million new cases in the world each year, breast cancer is the commonest malignancy in women and comprises 18% of all female cancers.

There is an international/geographical variation in the incidence of Breast Cancer. Incidence rates are higher in the developed countries than in the developing countries. Incidence rates are also higher in urban areas than in the rural areas [3]. In Africa, breast cancer has overtaken cervical cancer as the commonest malignancy affecting women and the incidence rates appear to be rising.

In the United Kingdom, where the age standardised incidence and mortality is the highest in the world, the incidence among women aged 50 approaches two per 1000 women per year, and the disease is the single commonest cause of death among women aged 40-50, accounting for about a fifth of all deaths in this age group. There are more than 14 000 deaths each year, and the incidence is increasing particularly among women aged 50-64, probably because of breast screening in this age group [4]. Screening aims to improve survival by decreasing the risk of metastases through the early detection of breast cancer. Thus, rate of survival with breast cancer have increased significantly all over the world in the past decades. Factors that increase the incidence of breast cancer include early menarche and late menopause, null parity and an increased age at the first birth. Also, family history of breast cancer before the age of 40, bilateral breast cancer, ovarian cancer are also associated with breast cancer [5].

Zare [6] worked on modeling of breast cancer prognostic factors using a parametric log-logistic model in Fars province, Southern Iran.The log-logistic model was employed as the best parametric model which could explain survival times. The hazard rates of the poor and the medium prognosis groups were respectively 13 and 3 times greater than in the good prognosis group. Also, the difference between the overall survival rates of the poor and the medium prognosis groups was highly significant in comparison to the good prognosis group.

## 2. BREAST CANCER IN NIGERIA

In the North-Western geopolitical zone of Nigeria, cancer of the breast was second to cancer of the cervix, while at University College Hospital (UCH), Ibadan (situated in the South-Western geopolitical zone of Nigeria) it was the leading

malignancy among women. In the North-Central geo-political zone, breast cancer constituted 22.41% of new cancer cases registered in 5 years and accounted for 35.41% of all cancers in women. Unfortunately there is paucity of data and sparse literature review on the trends of breast cancer in Nigeria due to few existing cancer registries most of which are either hospital-based or pathology based instead of the preferred population-based cancer registries. Also However, in low resource countries, hospital-based cancer registry has been serving as a fundamental source of information on cancer [7]. In Nigeria for example, incidence rate has increased from 13.8-15.3 per 100,000 in the 1980s, to 33.6 per 100,000 in 1992 and 116 per 100,000 in 2001. These increases in incidence are due to changes in the demography, socio-economic parameters, epidemiologic risk factors, late reporting and unawareness of the disease. While mortality rates are declining in the developed world (Americas, Australia and Western Europe) as a result of early diagnosis, screening, and improved cancer treatment programs, the converse is true in the developing countries [8].

In developing or low income countries, breast cancer was characterized by late clinical presentation and in advanced stage of the disease, when only chemotherapy and palliative care could be offered, and therefore associated with high mortality [9]. In Nigeria, as indeed in many developing countries, a combination of poor health education, poverty and a high patronage of non-orthodox healing practices among the populace contribute to late presentation of breast cancer in many hospitals with attendant high number of metastatic disease and poor disease survival. This is worsened by the commonly encountered non-adherence to treatment schedule among the patients. The burden of caring for these large numbers of patients in a low resource country is enormous [8]. Ina retrospective study carried out.

The purpose of this study is to predict survival times, contribution of prognostic factors and illustrate accelerator factor between early presentation and late presentation of patient of breast cancer patients.

## 3. THEORETICAL BACKGROUND (THE TYPE I GENERALIZED HALF LOGISTIC SURVIVAL MODEL)

Aalen [10] noted that parametric survival model is underused in medical research and deserving of more attention. In this section we introduce a parametric distribution called the type I generalized half logistic distribution. One of the probability distributions which is a member of the family of logistic distribution is the half logistic distribution with probability density function (pdf).

$$f(t) = \frac{2e^t}{(1+e^t)^2}$$

and cummulative distribution function (cdf)

$$F(t) = \frac{e^t - 1}{1 + e^t}$$

Balakrishnan [11] studied order statistics from the half logistic distribution, Balakrishnan and Puthenpura [12] obtained best unbiased estimates of the location and scale parameter of the distribution while Olapade [13] presented some theorems that characterized the distribution. Balakrishnan and Wong [14] obtained approximate maximum likelihood estimates for the location and scale parameters of the half logistic distribution. Torabi and Bagheri [15] presented an extended generalized half logistic distribution and studied different methods for estimating its parameters based on complete and censored data. Olapade [16] obtain a generalized form of half logistic distribution through a transformation of an exponential random variable called type I generalized half logistic distribution as

$$f(t) = \frac{\beta\, 2^{\beta}\, \mathrm{e}^{\frac{\mathrm{x}-\mu}{\sigma}}}{\left(1+\mathrm{e}^{\frac{\mathrm{x}-\mu}{\sigma}}\right)^{\beta+1}} \qquad \beta, \mu, \sigma > 0$$

He obtain the cumulative distribution function as

$$F(t) = 1 - \frac{2^{\beta}}{\left(1+\mathrm{e}^{\frac{\mathrm{x}-\mu}{\sigma}}\right)^{\beta}} \qquad \beta, \mu, \sigma > 0$$

Awodutire et al. [17] introduced the distribution derived by Olapade [16] to survival analysis in which he derived the survival function, hazard function and median survival time of the survival model were established. Estimation of the parameters of the model was done using the maximum likelihood method. The model was applied to a breast cancer data without covariates to establish it superiority performance over common existing survival models. For this study, the type I generalized half logistic survival model is applied to breast cancer survival data.

Here, the covariates are put under consideration, the accelerator factor between the early presentation and the late presentation is derived.

## 4. MATERIALS AND METHODS

### 4.1 Study Site

Ladoke Akintola University of Technology Teaching Hospital, Osogbo, the capital city of Osun state was established in 1991. It is located in Osun state in the South-Western part of Nigeria. It is jointly owned and funded by two states (Oyo state and Osun state).

### 4.2 Study Design

The study was a descriptive study conducted on breast cancer cases from 2009 to 2014. The study was carried out at the general surgery ward of the hospital. The type I generalized half logistic survival model was used to determine the effect of the prognostic factors towards the survival times of the patient and determine the accelerator factor between early reporting patients and late reporting patients.

### 4.3 Data Collection

Clinical data from eighty-nine selected breast cancer patients were retrieved from their case-note files in Ladoke Akintola University of Technology Teaching Hospital Osogbo. The survival times of the patients are retrieved from their files, censored at one year of diagnosis. The survival time recorded is the time from the day of report (admission) of the patient till the day of last contact (death, alive or loss to follow up). Also, variables (factors) that might influence the survival time of the patient were also recorded. The variables retrieved for this research are Age of Patients at report, Age of Patient at menarche, Use of Contraceptives, Average years used for breastfeeding, Stage of tumor development at point of report, use of Neoadjuvant Therapy. The data was analyzed using the type I generalized half logistic survival model with the aid of R-statistical software. The accelerated failure time model was determined. Akaike Information Criterion (AIC) was used for comparison with other common existing models.

## 5. RESULTS

### 5.1 Exploratory Data Analysis

The survival time distribution of the patients is skewed to the left as could be seen from Fig. 1. The skewness of this survival time distribution is pointing to the fact that as the survival time increases, the number of survivors decreases.

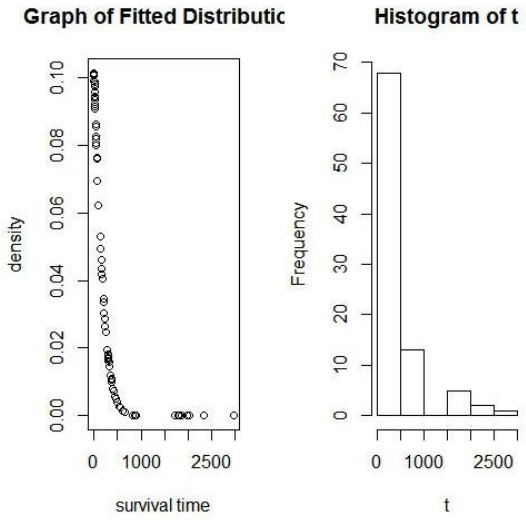


**Fig. 1. Histogram of the survival times of Breast cancer patients**

### 5.2 Parametric Estimation of the Survival Model

This parametric estimation estimates the parameters considering the covariates. Therefore, it estimates both the parameters of the distribution and the parameters of the explanatory variables.

Using the survival time data collected, with the aid of computer programming, the estimates of the parameters are shown in Table 1 and Table 2.

From the results from Table 2, two risk factors met the 0.05 significance criterion for statistical significance. They are age at menarche and stage at presentation.

From the Table 3, the type I GHL Survival model (with AIC value at 627.4) gives the smallest value and thus, is the best model when compared with the common existing ones.

### 5.3 The Median Survival Time

Awodutire et al. [17] derived the formula of the median survival time of the type I generalized half logistic survival model as

$$t_{0.5} = \mu + \sigma\left(\log\left(\sqrt[\alpha]{2}\,(2) - 1\right)\right)$$

**Table 1. Table displaying results of Type I generalized survival model**

| Parameter | Estimates | S.E | Z-value |
|---|---|---|---|
| Intercept | 0.02170473 | 0.02361312 | 0.9191809 |
| Age | 0.10851177 | 0.10045660 | 1.0801856 |
| Menarche | -0.90903224 | 0.16093547 | -5.6484270 |
| Breastfeed | 2.85565100 | 9.45606604 | 0.3019914 |
| Contraceptive | -0.36036744 | 0.46886076 | -0.7686023 |
| Presentation | -2.82065052 | 0.41984342 | -6.7183392 |
| neoadjuvant | 2.72633379 | 18.99434190 | 0.1435340 |
| mu | 396.86311260 | 54.16024961 | 7.3275717 |
| sigma | 586.18382460 | 82.45370651 | 7.1092477 |
| b | 10.66686098 | 5.34404983 | 1.9960257 |

**Table 2. Table displaying results of Type I generalized survival model**

| Parameter | LCL | UCL | P-value |
|---|---|---|---|
| Intercept | -0.001908392 | 0.045317852 | 0.358 |
| Age | 0.008055172 | 0.208968368 | 0.28 |
| Menarche | -1.0699677 | -0.7480968 | 0.00 |
| Breastfeed | -6.600415 | 12.311717 | 0.76 |
| Contraceptive | -0.8292282 | 0.1084933 | 0.44 |
| Presentation | -3.240494 | -2.400807 | 0.00 |
| neoadjuvant | -16.26801 | 21.72068 | 0.89 |
| mu | 342.7029 | 451.0234 | 0.00 |
| sigma | 503.7301 | 668.6375 | 0.00 |
| b | 5.322811 | 16.010911 | 0.046 |

**Table 3. Table displaying comparison of Type I GHL survival model with common existing models**

| Model | Loglikelihood | AIC |
|---|---|---|
| Type I GHL | -308.7 | 627.4 |
| Exponential | -374.3 | 762.6 |
| Lognormal | -337.9 | 691.8 |
| Loglogistic | -338.7 | 693.4 |
| Weibull | -341.9 | 699.8 |

Therefore, substituting values of σ, μand b derived from the Table 2, we have

$$t_{0.5} = 396.86 + 586.18(\ln(2^{\sqrt[10.67]{2}} - 1))$$
$$t_{0.5} = 471\ days$$

### 5.4 Accelerator Factor between the Early Reported Case and the Late Reported Case

To get the accelerated factor, we exponentiate the estimate of the parameter in question. For parameter stage of presentation, which indicates those who report early and those who report late, the accelerator factor is

Therefore

$$S_E(t) = S_L(0{:}0596t) \quad (9)$$

equivalently, in terms of survival times, this becomes

$$0{:}0596T_E = T_L{:} \quad (10)$$

which also gives,

$$T_E = 16{:}79T_L \quad (11)$$

## 6. CONCLUSION

In this paper, we applied the type I generalized half logistic survival model to model the survival times of breast cancer patient in a teaching hospital in Osogbo. The model is a predictive model of survival times, considering the prognostic factors. The result of the study showed that age at menarche of breast cancer patients and the stage of presentation (reporting) are significant at 0.05 significance level. Also, the accelerator factor shows that a day of survival of a late reported breast cancer case is equivalent to 16.79 days of the early reporting ones. This

means an early reporting patient will survive 16.79 times the late reporting ones. The Akaike Information Criteria (AIC) was used to compare the new model derived and the one gotten by Awodutire et al. [18] and this revealed that the type I generalized half-logistic survival model clearly demonstrates superiority.

## 7. RECOMMENDATION

It is recommended that breast cancer screening be conducted for patients who have early age at menarche presenting for treatment of any disease in the hospital. Also, we advocate for the government to promote breast cancer awareness practices among females, the need for early presentation of breast cancer cases as this will improve survival times of patients. The government should further help in making cancer registries functional in Nigeria to enhance proper documentation of cancer patients.

## CONSENT

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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